
Tobacco Use and Its Contribution to Early Cancer Mortality with a Special Emphasis on Cigarette Smoking

Donald R. Shopland

Smoking and Tobacco Control Program, National Cancer Institute, Bethesda, Maryland

This paper provides an overview of the relationship between tobacco use and early cancer mortality. It presents a retrospective examination of trends in smoking behavior and how these trends affected the national lung cancer mortality pattern during this century. Information on smoking prevalence is presented for black and white men and women for each 5-year birth cohort between 1885 and 1969. The author argues that the lung cancer mortality pattern observed in the United States since 1950 is entirely compatible with changes in smoking behavior among the various birth cohorts examined. The paper also reviews our current scientific knowledge about the etiological relationship between cigarette smoking and site-specific cancer mortality, with particular emphasis on lung cancer. Data on other forms of tobacco use and cancer mortality risks are included as are data on environmental tobacco smoke exposures and nonsmokers' lung cancer risk. Data are presented to demonstrate that cigarette use alone will be responsible for nearly one-third of the U.S. cancer deaths expected in the United States in 1995, or 168,000 premature cancer deaths. Among males, 38% of all cancer deaths are cigarette related, while among women 23% of all cancer deaths are due to cigarettes. These totals, however, include neither the cancer deaths that could reasonably be attributed to pipe, cigar, and smokeless tobacco use among males nor the estimated 3000 to 6000 environmental tobacco smoke-related lung cancer deaths that occur annually in nonsmokers. It is concluded that tobacco use, particularly the practice of cigarette smoking, is the single greatest cause of excess cancer mortality in U.S. populations. — *Environ Health Perspect* 103(Suppl 8):131–141 (1995)

Key words: cigarette smoking; tobacco use; tobacco consumption; lung cancer; cessation of smoking; smoking prevalence; pipe and cigar smoking; smokeless tobacco; environmental tobacco smoke; changes in smoking by birth cohort, race, and gender differences in smoking behavior; race and gender differences in lung cancer death rates

Introduction

This paper provides an overview, not a detailed summary, of our current scientific knowledge about the health effects of tobacco use, especially the practice of cigarette smoking as it relates to cancer. The data presented are largely drawn from a number of major reviews, including the National Cancer Institute's (NCI) new series of smoking and tobacco control monographs (1–4), the annual reports of the U.S. Surgeon General on the health consequences of smoking (5–12), the

periodic reports issued by the Royal College of Physicians in Great Britain (13–16), the World Health Organization (WHO) (17,18), and the 1986 Report of the International Agency for Research on Cancer (IARC) (19).

Tobacco Use during This Century

Despite that tobacco use has been a significant aspect of American culture for hundreds of years, the practice of inhaling cigarette smoke is a relatively recent phenomenon and only gained widespread acceptance during this century (20,21). Until the introduction in the United States of the first modern blended cigarette (Camels) in 1913, most tobacco was consumed in the form of chewing tobacco or smoked as cigars or in pipes (Figure 1). In 1900, for example, of the 7.5 pounds of tobacco consumed per capita, nearly half was consumed as chewing tobacco (3.5 lb); just 0.16 of a pound was consumed in the form of machine-made, mass-produced cigarettes (21–23). Concurrent with the introduction of the blended cigarette, the major cigarette manufacturers began application of newly developed mass marketing

and advertising practices that substantially increased consumer demand for these new tobacco products. Consumption of machine-made cigarettes increased rapidly during and immediately after World War I, so that by the mid-1930s more tobacco was being consumed in cigarettes than in all other forms of tobacco combined (23).

The practice of cigarette smoking substantially altered the risks associated with tobacco use compared with the use of other forms of tobacco, for it required the user to inhale the smoke in order to absorb a sufficient quantity of nicotine. By inhaling, the user directly exposed the lung and the cardiovascular system to a number of toxic and carcinogenic agents. It would not become scientifically known until decades later that the smoke from a single cigarette is composed of over 4000 different constituents, including nearly 60 agents that are known carcinogens, tumor promoters, or tumor initiators (6,11). It was this change in how tobacco was consumed during the first half of the 20th century that is largely responsible for the epidemic of lung cancer and other smoking-related cancers that occurred during the last half of the century (21).

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Address correspondence to Dr. Donald R. Shopland, Smoking and Tobacco Control Program, National Cancer Institute, Executive Plaza North, Room 241, 6130 Executive Blvd., MSC 7337, Bethesda, MD 20892-7337. Telephone: (301) 496-8679. Fax: (301) 496-8675.

Abbreviations used: ACS, American Cancer Society; U.S. EPA, U.S. Environmental Protection Agency; ETS, environmental tobacco smoke; IARC, International Agency for Research on Cancer; NCI, National Cancer Institute; U.S. PHS, U.S. Public Health Service; RR, relative risk; WHO, World Health Organization.

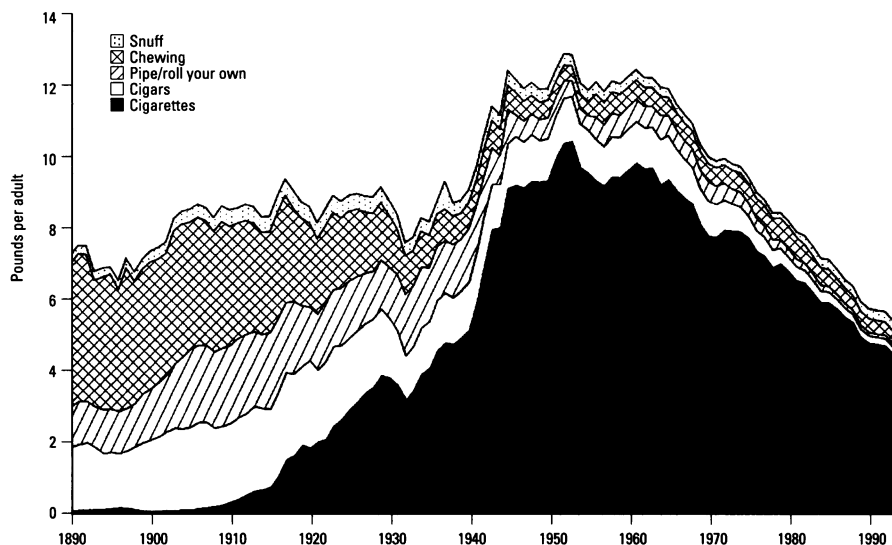


Figure 1. Trends in per capita tobacco consumption by major product category, United States, 1890 to 1994. Values expressed are pounds of tobacco consumed per year per adult (age 18 years and older) and represent unstemmed processing weight. Data from Shopland (21).

Smoking Behavior among Various Birth Cohorts of Men and Women

The rapid change from other forms of tobacco use to cigarettes did not occur uniformly across all major segments of the U.S. population. Social norms at the turn of the century limited tobacco use almost exclusively to males, with the exception of some limited snuff “sniffing” by women (7,22). In fact, cigarette smoking by large numbers of women would not become socially acceptable until cigarette advertising began to target women in the late 1920s and early 1930s (7,24).

Differences in smoking prevalence in women compared with men can be more easily explained by examining changes in smoking behavior among various birth cohorts over time. The data that follow are based on survey data collected by the National Center for Health Statistics from 1965 through 1991 as analyzed by Burns and colleagues and will be published in more detail in an NCI smoking and tobacco control monograph (24).

White Males

Figure 2 depicts smoking prevalence by 5-year age cohorts for white males born between 1885 and 1969. It is evident that the prevalence of smoking increases rapidly during adolescence, and the percentage of white males who became smokers increased for the first several cohorts shown. The

oldest cohorts (those born before 1900), however, have lower peak prevalence rates compared with those of successive cohorts. These individuals were already in early adulthood when cigarette manufacturers began using more sophisticated advertising and mass marketing techniques to promote their new machine-made cigarettes (just before World War I) and probably were less susceptible to such influences compared with those males born after 1900, who would have been subjected to such advertising and promotion influences while in their early teens (24).

White males born between 1900 and 1930 experienced similar patterns of initiation as well as peak smoking rates. A major characteristic of these older cohorts is the very broad area under each cohort curve, indicating that relatively little cessation occurred until much later compared with more contemporary age birth cohorts. In contrast, these later cohorts, while experiencing relatively high peak rates of smoking (some approaching 80%), have a much narrower plateau, and begin to decline almost as soon as their peak prevalence rate is reached.

White Females

Historically, patterns of smoking uptake and regular use by women have been very different from those of men. Until the mid-1920s when cigarette advertising began targeting women, very few women smoked. As advertising increasingly targeted women

during the 1930s and 1940s, cigarette use increased rapidly (7,24).

The pattern of initiation among white women, depicted in Figure 3, is strikingly different from that seen among their white male counterparts, especially those born before 1930. Among the most recent cohorts of women, initiation occurs largely during adolescence; however, among older cohorts (those born before 1940), initiation is much slower, and among the very oldest cohorts of women, smoking initiation continued well into their 30s and 40s.

There also are major differences between men and women with respect to their peak rate of smoking. Among the three oldest cohorts of white women (those born before 1900), no cohort achieved a 20% lifetime smoking rate, whereas every cohort of white males born between 1885 and 1954 experienced a 50% or higher peak rate—many achieving rates between 60 and 80%. Only among the two most recent birth cohorts are peak smoking rates comparable (24).

Black Males

Trends in smoking behavior among black men is similar to those observed among white men, although some differences are worth noting. Older cohorts of black men were somewhat less likely to become smokers than similar cohorts of white men and their age distribution for initiation is also somewhat older, indicating that compared with their white male counterparts, these cohorts have somewhat lower lifetime exposures to cigarette smoke. After 1915, however, every cohort of black males except for the most recent cohort (those born between 1965 and 1969) experiences a higher peak rate than white males (Figure 4). Furthermore, this greater current smoking rate experienced by most black male cohorts is the result of both a greater peak prevalence and a lower rate of decline in prevalence once their peak rate is achieved. In essence, this results in most black male cohorts having broader plateaus than their white male peers, indicating a longer duration of exposure to cigarette smoke, which helps explain their respective lung cancer mortality patterns during this century (21).

Black Females

In contrast to males, black and white females experience nearly identical patterns of smoking uptake and cessation. With the exception of differences in the age of initiation and lower rates of prevalence among the oldest cohorts of black women, the

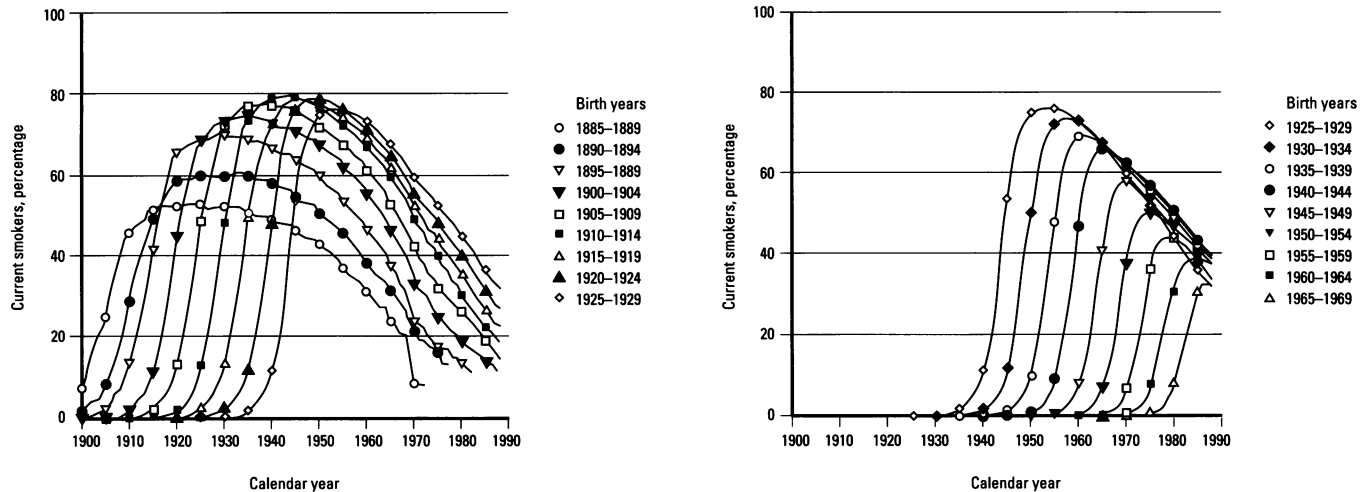


Figure 2. Current smoking prevalence by calendar year for 5-year birth cohorts of white males born between 1885 and 1969. Data from Burns et al. (24).

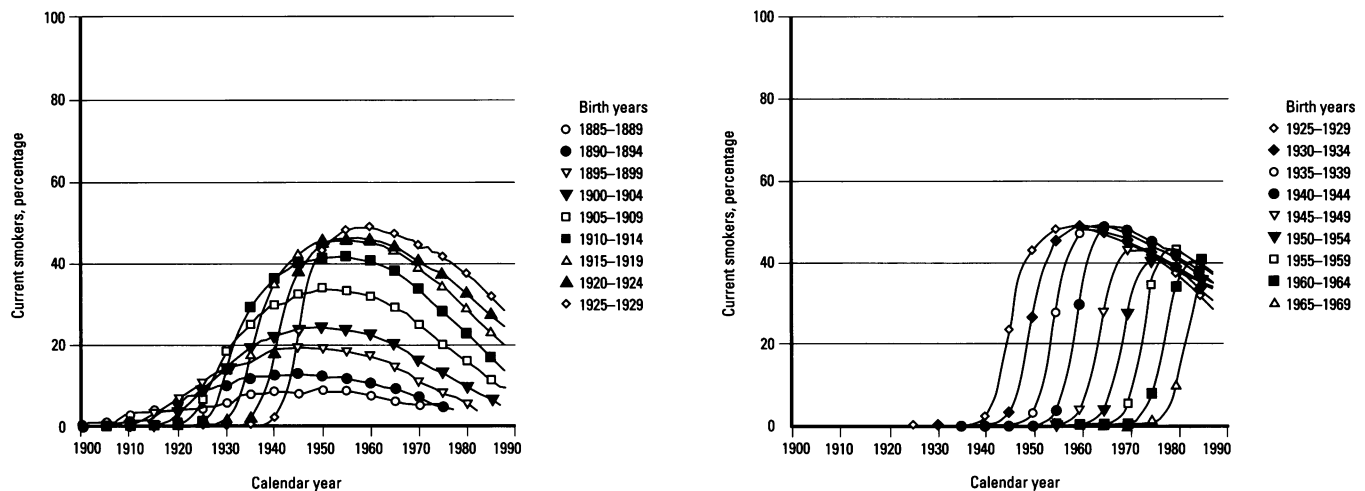


Figure 3. Current smoking prevalence by calendar year for 5-year birth cohorts of white females born between 1885 and 1969. Data from Burns et al. (24).

prevalence among most cohorts of black and white women is quite similar (Figure 5).

Influence of Smoking Patterns on Lung Cancer Mortality

As pointed out above, among the oldest birth cohorts of males (those born before 1915), whites experienced higher peak smoking rates and a somewhat earlier age of smoking initiation than their black male counterparts. After 1915, smoking rates among black male birth cohorts began to change, not only with respect to their peak smoking behavior but also with respect to the length of time (duration) each of these cohorts stayed at or close to their peak before declining.

White males began to change their behavior in the early 1950s when the first

scientific studies linking smoking and lung cancer were published (1,21,24). Other demographic groups were much slower to respond to this early information and did not begin to alter their behavior substantially until the mid-to-late 1960s following publication of the first U.S. Surgeon General's report in 1964 (5) and the broader public education campaigns of the late 1960s and early 1970s (25).

These changes in smoking behavior among various birth cohorts of black and white men and women largely explain the lung cancer mortality patterns observed in the United States throughout this century (1,21). Currently, black men experience the highest lung cancer death rates of any demographic group. However, until the early 1960s white males experienced the

highest death rates (26). This pattern is entirely consistent with the greater overall smoking exposures that occurred among those white (and not black) male cohorts born before World War I (21,24).

As black male cohorts with greater smoking exposures began to appear, and as white males began to modify their behavior, however, the national lung cancer mortality pattern began to change (Figure 6). Thus, in the early 1960s the black male age-adjusted lung cancer mortality rate exceeded that of whites and today is approximately 30% higher than the rate of their white male peers (27,28).

In contrast, only relatively small differences are seen between the overall smoking behavior of black and white women across individual birth cohorts during this century.

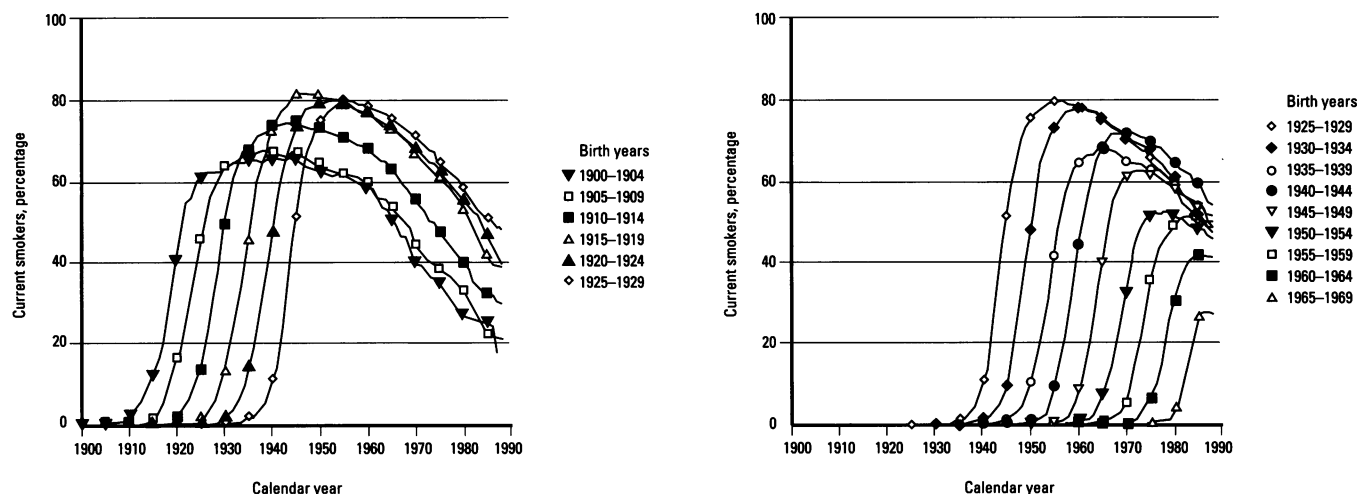


Figure 4. Current smoking prevalence by calendar year for 5-year birth cohorts of black males born between 1900 and 1969. Data from Burns et al. (24).

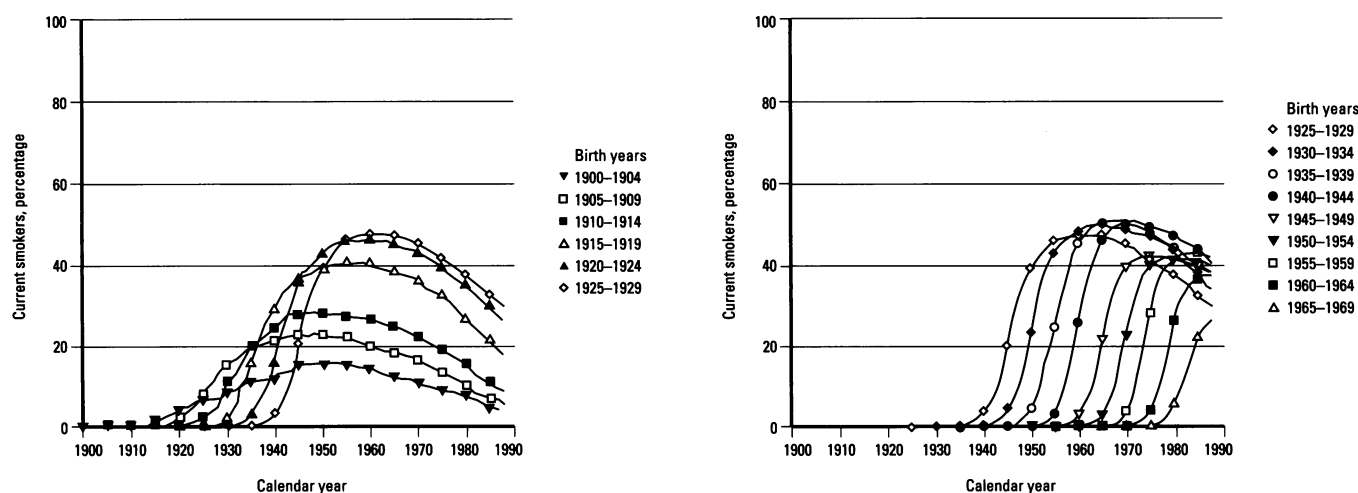


Figure 5. Current smoking prevalence by calendar year for 5-year birth cohorts of black females born between 1900 and 1969. Data from Burns et al. (24).

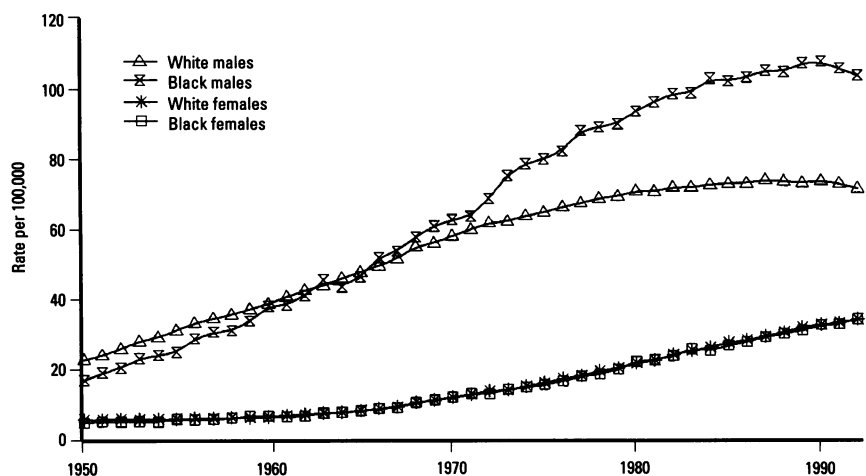


Figure 6. Age-adjusted lung cancer mortality rates by race and sex, United States, 1950 to 1992. Age adjusted to 1970 U.S. population. Data from Shopland (21).

As a result, the lung cancer mortality experience of black and white women has been nearly identical (27). In 1992, both the age-adjusted lung cancer mortality rate and the absolute number of lung cancer deaths among black women were projected to exceed those of breast cancer for the first time. It is likely, therefore, that lung cancer is now the leading cause of cancer death among black women in the United States, a phenomenon that occurred among white women in 1986 (27). Lung cancer has been the leading cause of cancer mortality among both black and white men for decades (26).

Cigarette Smoking and Early Cancer Mortality

A series of authoritative reports issued by the U.S. Surgeon General and others conclusively document that cigarette

smoking is causally related to a host of fatal diseases, including several major sites of cancer (1–19). A list of these diseases and their established epidemiologic associations with cigarette smoking is presented in Table 1 [based in part on Shopland and Burns (29)].

For some diseases, including four sites of cancer, cigarette smoking is the single largest contributor (defined as responsible for half or more of all deaths annually) to

Table 1. Causes of death and their established epidemiological association with cigarette smoking.

| Category | Cause of death |
|----------|--|
| A | Cancer of lung ^a |
| | Chronic obstructive pulmonary disease (includes emphysema) |
| | Peripheral vascular disease |
| | Cancer of larynx ^a |
| | Cancer of oral cavity (pharynx) ^a |
| B | Cancer of esophagus ^a |
| | Stroke |
| | Coronary heart disease |
| | Cancer of bladder ^a |
| | Aortic aneurysm |
| | Perinatal mortality |
| C | Cancer of cervix uteri ^a |
| | Leukemia (myeloid) ^a |
| | Gastric ulcer ^b |
| | Duodenal ulcer ^b |
| | Cancer of kidney ^a |
| | Cancer of pancreas ^a |
| | Cor pulmonale |
| | Cancer of stomach ^{a,b} |
| | Cancer of rectum ^a |
| | Cancer of colon ^a |
| D | Pneumonia ^b |
| | Cancer of the liver ^a |
| | SIDS |
| | Alcoholism |
| | Cirrhosis of liver |
| E | Poisoning |
| | Suicide |
| | Endometrial cancer ^a |
| | Parkinson's disease |
| | Ulcerative colitis |

A, diseases for which a direct causal association has been firmly established and smoking is considered the single, major cause, i.e., responsible for half or more of all deaths annually from the disease; B, diseases for which a direct causal association has been firmly established, but smoking is but one of known causes; C, diseases for which smokers experience higher death rates than nonsmokers, but the causal nature of the association has not been clearly elucidated (for some of these causes of death); D, causes of death for which excess mortality in smokers has been observed, but association is attributed to confounding; E, diseases that epidemiological studies have consistently found to have lower death rates in smokers than in nonsmokers.

^aNeoplastic disease sites now associated with cigarette smoking. ^bA causal association is considered highly probable.

excess mortality for these causes of death. In addition to these sites, cigarette smoking is an established cause of other cancers (category B in Table 1) and has been etiologically associated with several additional cancer sites (category C in Table 1), although for some sites the causal nature of this association has not been fully elucidated. Nonetheless, for each site listed in the table, the death rates among current smokers are greater than the death rates among comparable nonsmokers and for many a consistent dose-response trend has been observed. For one site, endometrial cancer (see category D in Table 1), studies have consistently shown that cigarette smoking is associated with a lower risk of mortality (9,11,12,30). The evidence is far from clear, however, as to whether smoking actually protects women from developing and dying from this cancer.

Cigarette Smoking and Site-Specific Cancer Mortality

The mortality risks among both current and former male and female smokers relative to nonsmokers for select cancer sites are presented in Table 2. These data are taken from the American Cancer Society (ACS) prospective study involving over 1.2 million people in all 50 states (11,31).

For each major cancer site listed, the mortality risk among current smokers is significantly higher than 1.0; the risks

Table 2. Relative risks for major smoking-related cancer sites among male and female smokers. ACS 50-State Study, 4-year follow-up.

| Cancer site | Current smokers ^a | Former smokers ^b |
|----------------|------------------------------|-----------------------------|
| Males | | |
| Lung | 22.36 | 9.36 |
| Oral | 27.48 | 8.80 |
| Esophagus | 7.60 | 5.83 |
| Larynx | 10.48 | 5.24 |
| Bladder | 2.86 | 1.90 |
| Pancreas | 2.14 | 1.12 |
| Kidney | 2.95 | 1.95 |
| Females | | |
| Lung | 11.94 | 4.69 |
| Oral | 5.59 | 2.88 |
| Esophagus | 10.25 | 3.16 |
| Larynx | 17.78 | 11.88 |
| Bladder | 2.58 | 1.85 |
| Pancreas | 2.33 | 1.78 |
| Kidney | 1.41 | 1.16 |
| Cervix | 2.14 | 1.94 |

^aCurrent cigarette smokers are individuals who reported they were smoking cigarettes regularly at time of enrollment in this study. ^bFormer cigarette smokers are individuals who reported they were not smoking at time of enrollment in this study but smoked cigarettes regularly in the past. Data from DHHS (11).

among former smokers are intermediate to those of current smokers and those who never smoked. Respiratory tract cancers are particularly elevated in smokers, which probably reflects the fact these sites are most exposed to the carcinogens known to exist in cigarette smoke (21). The risks of developing any of the smoking-related cancers is dose-related. That is, the greater the exposure to cigarette smoke, the greater the risk.

The risk for lung cancer is particularly worth noting, as lung cancer now accounts for nearly 30% of all cancer deaths annually in the United States (32). Lung cancer mortality risks among current smokers increase with increasing doses of cigarette smoke received, as measured by the number of cigarettes consumed daily, duration (years) of smoking, depth of inhalation, early age of initiation, and tar content of the brand smoked (4,5,9,11,19,29). Table 3 provides information by amount smoked taken from a number of the larger prospective studies; several of these represent non-U.S. populations. Many of these studies have also followed substantial numbers of women. Taken together, they represent over 20 million person-years of observation.

In the ACS 50-state study initiated in 1982, the lung cancer mortality ratios among male and female smokers, regardless of the amount smoked, are 22 and 12, respectively. As the number of cigarettes consumed increases, lung cancer mortality risks also increase. Males smoking more than a pack of cigarettes per day experienced a relative risk (RR) of 27; for women smoking 20 or more cigarettes (data not shown in table), the RR is 16. Data from the other studies show similar increases in risk with increasing daily consumption.

Various independent investigators and government reports have consistently estimated that cigarette use is responsible for between 80 and 90% of all lung cancer deaths annually in the United States (31,33–35). In those countries and cultures in which cigarette use has been an established behavior for many decades, lung cancer is also a significant cause of death and often is the dominate form of neoplastic disease in the population (36,37).

The Benefits of Smoking Cessation on Reduced Cancer Risk

While current cigarette smokers experience substantial early cancer mortality, especially for cancers of the head and neck, former cigarette smokers are observed to have reduced mortality compared with

Table 3. Lung cancer mortality ratios in men and women, by number of cigarettes smoked daily, major prospective mortality studies.

| Study, population | Men | | Women | |
|---------------------------------|-----------------|-------|-----------------|-------|
| | Cigarettes, day | Ratio | Cigarettes, day | Ratio |
| ACS 25-State Study, 1 million | Nonsmokers | 1.00 | Nonsmokers | 1.00 |
| | All smokers | 8.53 | All smokers | 3.58 |
| | 1–9 | 4.62 | 1–9 | 1.30 |
| | 10–19 | 8.62 | 10–19 | 2.40 |
| | 20–39 | 14.69 | 20–39 | 4.90 |
| | 40+ | 18.71 | 40+ | 7.50 |
| British Doctors' Study, 40,000 | Nonsmokers | 1.00 | Nonsmokers | 1.00 |
| | All smokers | 14.90 | All smokers | 5.00 |
| | 1–14 | 7.50 | 1–14 | 1.28 |
| | 15–24 | 14.90 | 15–24 | 6.41 |
| | 25+ | 25.40 | 25+ | 29.71 |
| U.S. Veterans' Study, 290,000 | Nonsmokers | 1.00 | | |
| | All smokers | 11.28 | | |
| | 1–9 | 3.89 | | |
| | 10–19 | 9.63 | | |
| | 21–39 | 16.70 | | |
| | 40+ | 23.70 | | |
| Japanese Study, 270,000 | Nonsmokers | 1.00 | Nonsmokers | 1.00 |
| | All smokers | 3.76 | All smokers | 2.03 |
| | 1–9 | 2.06 | 1–9 | 2.25 |
| | 10–19 | 4.00 | 10–19 | 2.56 |
| | 20+ | 6.24 | 20+ | 4.47 |
| ACS 50 State Study, 1.2 million | Nonsmokers | 1.00 | Nonsmokers | 1.00 |
| | All smokers | 22.36 | All smokers | 11.94 |
| | 1–20 | 18.80 | 1–10 | 5.50 |
| | 20+ | 26.90 | 11–19 | 11.20 |
| | | | 20 | 14.20 |
| | | | 21–30 | 20.40 |
| | | | 31+ | 22.00 |

Data from Doll et al. (44), Doll et al. (66), Hrubec et al. (69), Rogot et al. (71), Hammond (72), Hammond et al. (73), Hirayama (74), Garfinkel and Stellman (75), Thun et al. (76), Thun et al. (77).

Table 4. Relative risk of developing lung cancer by time since stopping smoking and total duration of smoking behavior.

| Time since stopping smoking, years | Duration of smoking habit | | | |
|------------------------------------|---------------------------|-------------|-------------|------------|
| | 1–19 years | 20–39 years | 40–49 years | > 50 years |
| Men | | | | |
| 0 | 1.0 ^a | 2.2 | 2.8 | 3.0 |
| 1–4 | 1.1 | 2.1 | 3.3 | 3.8 |
| 5–9 | 0.4 | 1.5 | 2.2 | 2.8 |
| 10+ | 0.3 | 1.0 | 1.6 | 2.7 |
| Women | | | | |
| 0 | 1.0 ^b | 2.1 | 2.7 | 5.2 |
| 1–4 | 1.0 | 2.3 | 2.1 | 7.1 |
| 5–9 | 0.4 | 2.0 | 1.1 | 1.7 |
| 10+ | 0.4 | 0.8 | 2.3 | |

^aBaseline category; risk for people who had never smoked relative to that for current smokers who had smoked for one to 19 years was 0.3. ^bBaseline category; risk for people who had never smoked relative to that for current smokers who had smoked for 1 to 19 years was 0.6. Data from Lubin et al. (38).

continuing smokers (9,11,12). For each of the major smoking-associated cancer sites, the risk among former smokers is lower compared to that found among current smokers, but their risk is still higher than those who never smoked (12).

The data for lung cancer clearly illustrate the benefit of quitting smoking. In a large

case-control study by Lubin and colleagues (38) involving over 7000 male and female lung cancer patients, the risks declined for both men and women with increases in the number of years off cigarettes, although among men the rate of decline was greater for those males who had smoked for the shorter length of time (Table 4). After 10

years off cigarettes, individuals who had smoked less than 20 years experienced a lung cancer risk similar to those who had never smoked. However, the risk remained high among both sexes who reported smoking for 20 years or more, regardless of the time reported off cigarettes (39).

In the ACS 50-state study, an attempt was made to examine the effect of health status on smoking cessation and its relationship to reduced lung cancer mortality (12). The lung cancer risk for those smokers who reported no history of heart disease, stroke or cancer at the time of enrollment were compared with those for all respondents (including those with and without a history of disease) by the length of time since quitting smoking and the number of cigarettes consumed daily. The data for both men and women are presented in Table 5.

Individuals who reported having quit smoking for 2 years or less and who had a history of chronic disease at time of enrollment in the study experienced lung cancer mortality risks that exceeded those of continuing smokers. In contrast, among those individuals (both men and women) who reported no history of chronic disease, lung cancer risk began to drop immediately following cessation of smoking. Among nearly 300,000 U.S. veterans, those who quit smoking because of doctor's orders experienced higher death rates than those who quit for reasons other than doctor's orders. It is likely that individuals who quit smoking because of existing disease or poor health status (possibly due to their smoking) do not derive the same benefit from stopping as those who quit out of concern for future health considerations.

In both studies, lung cancer risk decreased with increasing years of cessation of smoking; approximately 10 years following cessation, the lung cancer risk among former smokers was reduced by approximately half (29). These data also indicate, however, that a measurable risk is still apparent among former smokers who have been off cigarettes 16 years or more, and this risk was present even among smokers who reported smoking less than a pack per day (9,12,29).

For cancer of sites other than lung, individuals who quit smoking face lower risks of cancer than those individuals who continue to smoke (11). For example, quitting smoking approximately halves the risks for oral, esophageal, and bladder cancer within 5 years following cessation (12,29). The risk for pancreatic cancer is reduced in former smokers but may

only be measurable after 10 years or more of abstinence (12,29).

Pipe and Cigar Smoking

Regular use of pipes and cigars is associated with an increased risk of disease. In fact, these forms of tobacco smoking are highly correlated with cancers of the oral cavity, larynx, and esophagus (5,9,11,19). Both prospective and retrospective studies have consistently found that pipe and cigar smokers experience mortality risks from these sites that equal and sometimes exceed the risks found in cigarette smokers (9). Additionally, pipe and cigar smokers also experience higher lung cancer mortality risks than nonusers. In a large case-control study in Western Europe, compared to nonsmokers, risks for lung cancer among males smoking cigars only and pipes only were 2.5 and 2.9, respectively (40). There were significant trends of increased risk with years of use and with numbers of cigars and pipes smoked per day. The lower lung cancer risk among users of these products compared with that among cigarette smokers probably reflects the fact that "pure" pipe and cigar users (those who have only smoked these products and not cigarettes) do not report active inhalation of the smoke. Unfortunately, many life long cigarette smokers switch to pipes and cigars believing that by doing so they are lowering their risk of disease, but they often continue to inhale (41).

Public Health Burden of Cigarette Use on Cancer Mortality

A number of published estimates have appeared in the scientific literature in an attempt to depict the cancer burden attributed to cigarette use in the United States (9,31,33-35,42). In general, these studies have demonstrated that approximately one-third of all cancer deaths annually can be reasonably attributed to cigarette smoking. In an analysis previously published, NCI and ACS investigators estimated that cigarette smoking was responsible for about 157,000 of the 514,000 cancer deaths expected to occur in the United States in 1991, or about 31% of all cancer deaths that year (31). These totals, however, did not consider those cancer deaths that could be attributed to the pipe and cigar smoking among men, the contribution of smokeless tobacco use to oral cancer mortality, or those lung cancer deaths among nonsmokers that resulted from exposure to environmental tobacco smoke.

Table 5. Standard mortality ratios of lung cancer among former smokers in ACS-CPS II (relative to those who had never smoked) by years of smoking abstinence, daily cigarette consumption at time of cessation, and history of chronic disease.

| | No history of chronic disease | | All respondents | |
|-------------------------------------|-------------------------------|--------------------|---------------------|--------------------|
| | 1-20 cigarettes/day | ≥21 cigarettes/day | 1-20 cigarettes/day | ≥21 cigarettes/day |
| Males | | | | |
| Current smokers | 23.5 | 31.5 | 18.8 | 26.9 |
| Former smokers, years since stopped | | | | |
| <1 | 16.8 | 23.4 | 26.7 | 50.7 |
| 1-2 | 16.7 | 25.3 | 22.4 | 33.2 |
| 3-5 | 19.7 | 20.5 | 16.5 | 20.9 |
| 6-10 | 8.6 | 14.2 | 8.7 | 15.0 |
| 11-15 | 6.3 | 13.6 | 6.0 | 12.6 |
| ≥16 | 3.3 | 5.3 | 3.1 | 5.5 |
| Females | | | | |
| Current smokers | 10.5 | 24.1 | 7.3 | 16.3 |
| Former smokers, years since stopped | | | | |
| <1 | 3.4 | 21.1 | 7.9 | 34.3 |
| 1-2 | 9.0 | 18.2 | 9.1 | 19.5 |
| 3-5 | 2.5 | 13.2 | 2.9 | 14.6 |
| 6-10 | 1.1 | 12.0 | 1.0 | 9.1 |
| 11-15 | 1.1 | 2.9 | 1.5 | 5.9 |
| ≥16 | 1.6 | 2.4 | 1.4 | 2.6 |

Data from DHHS (12).

Table 6 provides an updated estimate of the 1995 cancer burden from cigarette smoking for the United States. The data in this table are based on cancer mortality projections published annually by the ACS (32). The percent attributable risk is derived using a standard attributable risk methodology for two levels of exposure (43) using smoking prevalence estimates from the National Health Interview Survey, conducted by the National Center for Health Statistics. In 1993, 27.7% of adult men and 22.5% of adult women were classified as current smokers; 29.9% of men and 19.7% of women were former smokers. Nearly 60% of women (57.8%) never smoked compared with 42.4% of men.

In this analysis we limited the data to the same eight major cancer sites previously mentioned (31) that have been traditionally considered causally related to cigarette smoking, although clearly additional cancer sites could have been included. Thus, the smoking attributed fraction should be considered conservative. This method produces an estimate of 168,057 cigarette-only excess cancer deaths in 1995 of 547,000 total cancer deaths expected. The term "excess" deaths is used in the sense that these deaths would not have occurred if cigarette smokers experienced the same death rates as nonsmokers. While the vast majority of the smoking-related excess deaths are due to

Table 6. 1995 U.S. cancer deaths caused by cigarette smoking.

| Site and ICD disease category | 1995 cancer deaths expected | Smoking attributable risk, % | Estimated deaths due to smoking |
|---|-----------------------------|------------------------------|---------------------------------|
| Males | | | |
| Oral,140-149 | 5,480 | 90.6 | 4,965 |
| Esophagus,150 | 8,200 | 76.6 | 6,282 |
| Pancreas,157 | 13,200 | 25.9 | 3,419 |
| Larynx,161 | 3,200 | 79.6 | 2,547 |
| Lung,162 | 95,400 | 89.4 | 85,288 |
| Bladder,188 | 7,500 | 43.8 | 3,285 |
| Kidney,189 | 7,100 | 45.1 | 3,202 |
| Total cancer deaths expected | 289,000 | | 108,988 |
| Females | | | |
| Oral,140-149 | 2,890 | 58.5 | 1,691 |
| Esophagus,150 | 2,700 | 71.5 | 1,931 |
| Pancreas,157 | 13,800 | 31.0 | 4,278 |
| Larynx,161 | 890 | 85.5 | 761 |
| Lung,162 | 62,000 | 76.1 | 47,182 |
| Cervix,180 | 4,800 | 30.6 | 1,469 |
| Bladder,188 | 3,700 | 34.2 | 1,265 |
| Kidney,189 | 4,600 | 10.7 | 492 |
| Total cancer deaths expected | 258,000 | | 59,069 |
| Total male and female cancer deaths expected in 1995 | | | 547,000 |
| Total excess deaths due to cigarette smoking | | | 168,057 |
| Percent of cancer deaths due to cigarette smoking in 1995 | | | 30.7 |

respiratory tract cancers, especially cancer of the lung, a significant number of excess deaths occur in other sites. The data also indicate that the cigarette-attributable fraction (percent) has remained relatively constant over time for both men and women, at around 38 and 23%, respectively.

Just as important, many of these sites have extremely poor 5-year survival rates and have changed little in absolute terms over the past 25 years (31). Only about 12% of all patients diagnosed with lung cancer survive 5 years, and the survival rates for cancers of the pancreas and esophagus are even more dismal (27,32).

Cigarette Smoking and Overall Cancer Mortality

Because of the large number of cancer sites associated with smoking, it's not surprising that the overall cancer risk in smokers compared with that in nonsmokers is substantially elevated. In the ACS 50-State study, which followed 1.2 million men and women for 6 years, male smokers, regardless of the amount smoked, experienced overall cancer mortality risks that were 350% higher than those of nonsmokers (3.50 RR); the risk for women who smoked was nearly 200% greater (1.86 RR) (4). Among 34,000 male British physicians followed prospectively for 40 years, Doll et al. observed an overall cancer mortality risk more than 200% greater among current smokers, and this risk increased as amounts smoked daily increased (44). Similar findings have been observed in other cohort studies published to date. If the cancer burden attributed to cigarette smoking presented in Table 6 were based on overall cancer mortality ratios rather than on the individual cause-specific mortality rates, the total number of excess cancer deaths would easily approach 200,000 annually.

Smokeless Tobacco Use as a Cause of Cancer

Until recently, little public health attention was focused on chewing tobacco or snuff use (commonly referred to as smokeless tobacco), as it constituted only a very small percentage of all tobacco consumed. Furthermore, until the mid-1970s, both total consumption and prevalence of use for both these products were declining (2,45). These trends began to reverse coincident with the introduction and mass marketing of new forms of snuff—moist snuff, to be specific, which is sold under such brand names as Skoal, Copenhagen, Happy Days, and Red Man (2).

Unlike cigarette advertising, which was banned from the public airways by the U.S. Congress in 1971 (46), advertisers of smokeless tobacco until recently have been free to use radio and television to promote their products. Until Congress extended the ban to include smokeless tobacco in 1987 (47), these products were heavily advertised on television, by famous athletes such as running backs Walt Garrison of the Dallas Cowboys and Earl Campbell of the Houston Oilers, baseball star George Brett, and well-known entertainers such as country and western star Charlie Daniels (2). As a result, consumption of moist snuff increased rapidly. In the 10-year period between 1982 and 1992, total snuff consumption in the United States increased by 12 million pounds (from 44 million to 56 million pounds), with moist snuff accounting for nearly all of this increase (48).

More important, the group that experienced the greatest increase in smokeless tobacco use was adolescents and young adults (49). This increase has been directly attributed to the youth-related advertising themes and messages used during this period of time. Television was the primary mode of such advertising, which often appeared during sports events or during prime-time viewing hours (2). Today about 6% of all males 18 years and older are regular users of smokeless tobacco; a significant proportion of this number is under the age of 30 (35) (Table 7).

Table 7. Smokeless tobacco use among adult males, age 18 and older, by product category, United States, 1970 and 1991.

| Product category | 1970 | 1991 |
|-----------------------|------|------|
| Chewing tobacco | | |
| Age: 18–24 | 1.8 | 4.1 |
| 25–34 | 2.2 | 3.1 |
| 35–44 | 3.3 | 2.5 |
| 45–64 | 4.2 | 2.4 |
| ≥ 65 | 9.4 | 3.9 |
| Total | 3.9 | 3.1 |
| Snuff | | |
| Age: 18–24 | 0.7 | 6.2 |
| 25–34 | 0.5 | 4.8 |
| 35–44 | 0.8 | 2.9 |
| 45–64 | 1.8 | 1.4 |
| ≥ 65 | 4.0 | 2.2 |
| Total | 1.5 | 3.3 |
| Any smokeless tobacco | | |
| Age: 18–24 | 2.2 | 8.4 |
| 25–34 | 2.5 | 6.9 |
| 35–44 | 3.9 | 4.9 |
| 45–64 | 5.8 | 3.7 |
| ≥ 65 | 12.7 | 5.6 |
| Total | 5.2 | 5.6 |

Data from CDC (35).

A number of epidemiological investigations were initiated concurrent with this rapid increase in consumption to assess whether use of smokeless tobacco was harmful. In 1981, Winn and colleagues (50) investigated the risks of snuff use on the incidence of oral and pharyngeal cancer among 255 women in North Carolina. The investigators found a 4-fold increase in risk among nonsmoking women who dipped snuff. For cancers of the gum and buccal mucosa, a strong dose–response effect was observed when measured by duration of use (Table 8).

Two major reviews on the health consequences of smokeless tobacco use, both of which cite U.S. as well as international studies, found similar results (45,51). The 1986 report of the Public Health Service (PHS) Advisory Committee to the U.S. Surgeon General (45) stated:

After a careful examination of the relevant epidemiologic, experimental, and clinical data, the committee concludes that the oral use of smokeless tobacco represents a significant health risk. It is not a safe substitute for smoking cigarettes. It can cause cancer and a number of noncancerous oral conditions and can lead to nicotine addiction and dependence.

Both reviews concluded that the evidence was strong that snuff use, particularly moist snuff, was a cause of cancer in humans, but the evidence for chewing tobacco was less clear.

No estimates exist to demonstrate the cancer burden that might reasonably be attributed to smokeless tobacco use. However, given the magnitude of the disease risks associated with smokeless tobacco use, especially for cancers of the oral cavity, there is no doubt that regular use of smokeless tobacco contributes some additional cancer cases and deaths annually.

Table 8. Estimated relative risk of oropharyngeal cancer according to duration of snuff use and anatomic site.

| Anatomic site | Duration of snuff use, years | Relative risk estimate |
|-------------------------|------------------------------|------------------------|
| Gum and buccal mucosa | 0 | 1.0 |
| | 1–24 | 13.8 |
| | 25–49 | 12.6 |
| | ≥ 50 | 48.0 |
| Other mouth and pharynx | 0 | 1.0 |
| | 1–24 | 1.7 |
| | 25–49 | 3.8 |
| | ≥ 50 | 1.3 |

Data from Winn et al. (50).

Furthermore, given the relatively recent rise in moist snuff use by adolescents—moist snuff is the most dangerous form of smokeless tobacco—public health officials have voiced concern that an increased incidence of oral cancer may arise as this bolus of new users ages (2,52). Just as the lung cancer epidemic did not begin until some 25 to 30 years following the large-scale uptake and regular use of cigarettes around World War I, the next tobacco-related epidemic could well be oral cancers during the early part of the 21st century (2).

Environmental Tobacco Smoke and Lung Cancer in Nonsmokers

By the beginning of the 1960s, the evidence linking cigarette smoking to early lung cancer mortality was overwhelming. By the time the Advisory Committee to the Surgeon General issued its now-famous report in 1964, more than 60 retrospective and prospective studies documenting this association existed in the scientific literature. For lung cancer, a measurable elevation in risk was consistently seen in those individuals who reported being only light or occasional cigarette smokers or who reported not inhaling during smoking (3). This elevation in risk, at relatively low exposure levels, prompted some public health officials to question whether the levels of tobacco smoke to which most nonsmokers were being exposed could also pose a health threat (53).

In 1971 then-Surgeon General Jesse Steinfeld directed that a complete review of the topic be prepared for the next Surgeon General's report (54). At that time no direct epidemiological evidence existed linking environmental tobacco smoke (ETS) to chronic disease health risks in nonsmokers. However, in the early 1970s the first epidemiological studies appeared documenting that infants and young children exposed to ETS experienced higher rates of respiratory problems, including hospital admissions for respiratory tract infections, than children from nonsmoking households (55).

In 1981, two studies were published—from Japan and Greece—showing a statistically significant elevation in lung cancer among never-smoking wives married to smoking husbands (56,57). Both studies also observed a greater lung cancer risk among those nonsmoking women whose husbands were classified as heavy smokers. A U.S. prospective study published later

that same year was also positive but not statistically significant (58).

By the time the National Academy of Sciences and the U.S. Surgeon General issued their independent assessments in 1986 (10,59), a total of 13 epidemiological studies existed in the peer-reviewed literature on ETS and lung cancer in nonsmokers. Most studies (11 of 13) demonstrated a positive association, and in 6 the risk was significant. Both reports concluded that ETS was a cause of lung cancer in nonsmokers.

In 1990 the U.S. Environmental Protection Agency (U.S. EPA) undertook the most complete review of this question. By the time the U.S. EPA issued its report, "Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders," 30 epidemiological studies were available for analysis (3). The 30 studies reviewed comprised more than 3,000 lung cancer cases from eight different countries and employed a wide variety of study designs and protocols (Table 9).

Twenty-four of 30 studies reported a higher risk of lung cancer among never-smokers ever exposed to ETS, and 9 were statistically significant. Furthermore, every 1 of the 17 studies that categorized risk by level of spousal smoking showed an increased risk among those most heavily exposed, and 9 were statistically significant in spite of most having low statistical power to detect an increase. Of the 14 studies for which dose-response trends could be tested, 10 were statistically significant—a result that would occur by chance less than 1 in 1 billion (3).

In conducting a formal risk assessment to establish the carcinogenic potential of a low-level exposure to an environmental agent, it is rare to have such a large epidemiologic base upon which to make scientific judgments. It is especially rare when the population data being examined

are based on actual levels of exposure that people encounter in their everyday activities. This is in sharp contrast to other risk assessments for which the only epidemiologic data are from populations with histories of very high occupational exposures to an agent (for example, asbestos workers and uranium miners) and the risk estimates at low exposures are extrapolated on the basis of mathematical models. Of all the agents U.S. EPA has classified as a Group A (known human carcinogen), ETS is the only agent for which an increased cancer risk has actually been observed at typical environmental levels of exposure (3).

ETS is also a significant source of preventable cancer mortality. U.S. EPA estimates that ETS exposure is responsible for approximately 3,000 nonsmoker lung cancer deaths annually. This is approximately the number of lung cancer deaths that U.S. EPA estimates to be attributable to indoor radon exposure and is at least an order of magnitude higher than the number of cancer deaths U.S. EPA attributes to nonoccupational asbestos exposure in our homes, worksites, and schools (60,61).

Two British investigators have estimated that living or working in buildings containing asbestos is associated with an annual risk of lung cancer of less than 1 in 1,000,000, a rate deemed unacceptable, as evidenced by the efforts made to remove asbestos from workplaces, schools, and other public buildings (62). These same investigators state that the relative risk for lung cancer due to ETS "is more than 100 times higher than the estimated effects of 20 years' exposure to the amount of chrysotile asbestos normally found in asbestos containing buildings" (63).

In summary, tobacco use, especially the practice of cigarette smoking, is the single largest contributor to cancer mortality in the United States, and is responsible for nearly one-third of all cancer deaths annually; 38% of all male and 23% of all female cancer deaths are directly related to cigarette use.

Cigarette smoking increases the death rate in smokers for at least 14 individual sites, and for several, cigarette smoking contributes to half or more of all such deaths annually. Of these, lung cancer is clearly the most important because of its significant impact on national cancer vital statistics.

Pipe and cigar smoking is not without significant disease risk; regular users of such products experience increased risks for several sites of cancer, especially cancer of

Table 9. ETS and lung cancer: pooled data by country, results from 30 studies.

| Country and number of studies | Overall risk ^a | High relative risk ^a |
|-------------------------------|---------------------------|---------------------------------|
| Greece (2) | 2.01 | 2.15 |
| Hong Kong (4) | 1.48 | 1.68 |
| Japan (5) | 1.41 | 1.96 |
| United States (11) | 1.19 | 1.38 |
| Western Europe (4) | 1.17 | 3.11 |
| China (4) | 0.95 | 2.32 |
| All studies combined | 1.30 | 1.81 ^b |

^aAll relative risk is adjusted for smoker misclassification. ^b $p < 0.000001$. Data from U.S. EPA (3).

the oral cavity. Pipe and cigar smokers are also at increased risk for cancers of the larynx, esophagus, and lung.

Use of smokeless tobacco, especially newer forms of moist snuff, is carcinogenic to humans. Long-term users experience up to a 50-fold increased risk for cancers of the cheek and gum compared with nonusers.

Environmental tobacco smoke is now an established cause of lung cancer in non-smokers and has been labeled a Group A (known human) carcinogen by the U.S. EPA. ETS is the only agent ever classified as a Group A carcinogen for which the increased cancer risks were based on typical environmental levels of exposure. Between 3,000 and 6,000 lung cancer

deaths annually are attributed to ETS exposures in nonsmokers.

Were it not for the historically high tobacco use rates observed in the United States during this century, we could be witnessing a decline in the overall cancer death rate instead of the small but persistent increases noted over the past 50 years.

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